

AMENDMENT AND RESPONSE TO OFFICE ACTION

Amendment

In the Claims

1. (currently amended) A multiparticulate milnacipran composition for oral administration comprising particles consisting of milnacipran complexed with an ion-exchange resin, wherein the composition provides delayed and extended release of milnacipran to produce a therapeutic effect over approximately 24 hours when administered to a patient in need, with diminished incidence or reduced intensity relative side effects resulting from administration of the same dose of milnacipran administered in an immediate release formulation.
2. (original) The composition of claim 1 wherein the ion-exchange resin particles are less than about 2 millimeter in diameter.
3. (original) The composition of claim 1 wherein the ion-exchange resin particles are less than about 500 microns in diameter.
4. (original) The composition of claim 1 wherein the ion-exchange resin particles are less than about 150 microns in diameter.
5. (canceled)
6. (canceled)
7. (canceled)
8. (original) The composition of claim 1 wherein the particles are enteric coated-extended release particles, prepared by coating extended release drug particles with an enteric coating.

9. (canceled)

AMENDMENT AND RESPONSE TO OFFICE ACTION

10. (canceled)

11. (withdrawn) The composition of claim 1 formulated into a dosage form selected from the group consisting of a gel, capsule, soft gelatin capsule, tablet, chewable tablet, crushable tablet, rapidly dissolving tablet, and unit of use sachet or capsule for reconstitution.

12. (original) The composition of claim 1 formulated into a liquid or liquid suspension.

13. (canceled)

14. (canceled)

15. (currently amended) The milnacipran composition of claim 14 1, wherein the side effect is nausea.

16. (withdrawn) The milnacipran composition of claim 14, wherein the side effects are selected from the group consisting of vomiting, headache, tremulousness, anxiety, panic attacks, palpitations, urinary retention, orthostatic hypotension, diaphoresis, chest pain, rash, weight gain, back pain, constipation, vertigo, increased sweating, agitation, hot flushes, tremors, fatigue, somnolence, dyspepsia, dysoria, nervousness, dry mouth, abdominal pain, irritability, and insomnia.

17. (currently amended) The milnacipran composition of claim 14 1 ~~having a milnacipran release profile that is characterized by release of~~ wherein less than approximately 20% of the total milnacipran dose ~~over a period up to two hours, followed by a slow or extended drug release~~ is released in one hour when the formulation is subjected to *in vitro* dissolution in

0.1 N HCl.

45083698

AMENDMENT AND RESPONSE TO OFFICE ACTION

18. (currently amended) The milnacipran composition of claim 17 wherein the defined milnacipran is released over a period of time that is between approximately four and approximately twenty-four hours.

19. (original) The composition of claim 1 further comprising one or more additional active ingredients.

20. (original) The composition of claim 19 wherein the active ingredients are selected from the group consisting of analgesics, anti-inflammatory drugs, antipyretics, antidepressants, antiepileptics, antihistamines, antimigraine drugs, antimuscarinics, anxiolytics, sedatives, hypnotics, antipsychotics, bronchodilators, anti asthma drugs, cardiovascular drugs, corticosteroids, dopaminergics, electrolytes, gastro-intestinal drugs, muscle relaxants, nutritional agents, vitamins, parasympathomimetics, stimulants, anorectics, and anti-narcoleptics.

21. (currently amended) The composition of claim 1 in a dosage form delivering a ~~dosage equivalent~~ therapeutically equivalent dose of between 5 and 500 mg milnacipran.

22. (currently amended) The composition of claim 21 in a dosage form delivering a ~~dosage equivalent~~ therapeutically equivalent dose of between 100 and 400 mg milnacipran.

23. (withdrawn) The milnacipran composition of claim 1, wherein the milnacipran is in the form of a therapeutically equivalent dose of either dextrogyral or levrogyral enantiomers of the milnacipran.

24. (original) The milnacipran composition of claim 1, wherein the milnacipran is in the form of a therapeutically equivalent dose of a mixture of milnacipran enantiomers.

AMENDMENT AND RESPONSE TO OFFICE ACTION

25. (withdrawn) The milnacipran composition of claim 1, wherein the milnacipran is in the form of a therapeutically equivalent dose of the active metabolite of milnacipran.

26. (withdrawn) The milnacipran composition of claim 1, wherein the milnacipran is in the form of a therapeutically equivalent dose of para-hydroxy-milnacipran (F2782).

27. (original) A method of treating a patient in need thereof comprising administering to the patient the composition of claim 1.

28. (currently amended) A method of making an oral formulation of milnacipran as defined by claim 1, comprising complexing milnacipran with ion-exchange resin particles and, ~~optionally~~, coating the drug particles with one or more polymer layers.

29. (new) The milnacipran composition of claim 1 wherein less than approximately 20% of the total milnacipran dose is released in two hours when the formulation is subjected to *in vitro* dissolution in 0.1 N HCl.